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Abstract: In eight anaesthetized closed-chest dogs, acute myocardial ischaemia was produced for 30 to 90 s by inflating a small balloon-catheter, which had been advanced transaortically into the periphery of the left anterior descending coronary artery. Left ventricular high-fidelity pressure measurements and simultaneous angiocardiography were carried out at control and during ischaemia. Left ventricular systolic function was assessed by the left ventricular ejection fraction (EF) as well as by regional shortening in a basal (SH M1), middle (SH M2 and apical (SH M3) segment. Diastolic function was evaluated by the stress-strain relationship using a viscoelastic model. Regional wall stiffness (Kn) was determined in the same three segments (basal, middle and apical), which were used for the evaluation of regional systolic function. For the interindividual comparison of the diastolic stiffness parameters normalization of the strain data was performed by calculating a reference wall circumference (I0) at a common wall stress of 1000 dynes/cm2. During localized myocardial ischaemia left ventricular end-diastolic pressure remained essentially unchanged (7.2 v. 8.3 mm Hg: NS). Left ventricular EF (47 v. 31% $P < 0.001$), SH M2 (27 v. 14 % $P < 0.005$) and SH M3 (22 v. 2% $P < 0.02$) decreased during ischaemia. Kn in the middle (10.0 v. 14.2; $P < 0.02$) and the apical (9.8 v. 12.7, $P < 0.005$) segment increased during ischaemia whereas Kn in the non-ischaemic basal segment remained unchanged (9.6 v. 11.8; NS). During ischaemia I0 increased in the middle segment (15.7 v. 17.3 cm; $P < 0.005$). Our data indicate that during acute ischaemia regional myocardial wall stiffness is increased in the ischaemic segment, but is normal in the non-ischaemic segment. Reference midwall circumference at a common wall stress of 1000 dynes/cm2 is enhanced during acute ischaemia (creep) and corresponds with the increased sarcomere length reported in ischaemic myocardium. Thus, it is suggested that the changes in regional myocardial wall stiffness are related to changes in reference midwall circumference with creep

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Regional wall stiffness during acute myocardial ischaemia in the canine left ventricle*

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KEY WORDS: Wall stiffness, creep, sarcomere length.

In eight anaesthetized closed-chest dogs, acute myocardial ischaemia was produced for 30 to 90 s by inflating a small balloon-catheter, which had been advanced transaortically into the periphery of the left anterior descending coronary artery. Left ventricular high-fidelity pressure measurements and simultaneous angiocardiography were carried out at control and during ischaemia. Left ventricular systolic function was assessed by the left ventricular ejection fraction (EF) as well as by regional shortening in a basal (SH M_1), middle (SH M_2) and apical (SH M_3) segment. Diastolic function was evaluated by the stress-strain relationship using a viscoelastic model. Regional wall stiffness (K_n) was determined in the same three segments (basal, middle and apical), which were used for the evaluation of regional systolic function. For the interindividual comparison of the diastolic stiffness parameters normalization of the strain data was performed by calculating a reference wall circumference (l_o) at a common wall stress of 1000 dynes/cm².

During localized myocardial ischaemia left ventricular end-diastolic pressure remained essentially unchanged (7·2 v. 8·3 mm Hg; NS). Left ventricular EF (47 v. 31%; P < 0·001), SH M_2 (27 v. 14%; P < 0·005) and SH M_3 (22 v. 2%; P < 0·02) decreased during ischaemia. K_n in the middle (10·0 v. 14·2; P < 0·02) and the apical (9·8 v. 12·7, P < 0·005) segment increased during ischaemia whereas K_n in the non-ischaemic basal segment remained unchanged (9·6 v. 11·8; NS). During ischaemia l_o increased in the middle segment (15·7 v. 17·3 cm; P < 0·005).

Our data indicate that during acute ischaemia regional myocardial wall stiffness is increased in the ischaemic segment, but is normal in the non-ischaemic segment. Reference midwall circumference at a common wall stress of 1000 dynes/cm² is enhanced during acute ischaemia (creep) and corresponds with the increased sarcomere length reported in ischaemic myocardium. Thus, it is suggested that the changes in regional myocardial wall stiffness are related to changes in reference midwall circumference with creep.

In man, regional wall motion abnormalities induced by myocardial ischaemia are generally sufficient to impair overall left ventricular systolic function[1, 2, 3]. The decrease in systolic function is accompanied by an increase in the left ventricular end-diastolic pressure and volume. However, it has been shown that the increase in end-diastolic pressure is higher than the increase in end-diastolic volume could explain[4, 5]. Therefore, several other mechanisms, which contribute to the increase in end-diastolic pressure, have been discussed, such as altered diastolic myocardial properties, impaired left ventricular relaxation, pericardial constriction, altered right ventricular loading conditions or changes in coronary artery perfusion[6, 7, 8].

The present study was designed to examine left ventricular diastolic properties during acute myocardial ischaemia in the canine model. One major point of the study was the assessment of regional left ventricular diastolic dynamics at a similar left ventricular end-diastolic pressure in both the control and the ischaemic state, in order to eliminate pericardial constriction and altered right ventricular loading conditions.

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Material and methods

Experiments were carried out in eight mongrel

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dogs with an average body weight of 27·4 kg. Cardiac catheterization was performed under general anaesthesia with alpha-chloralose i.v. in a dose of 90 mg/kg body weight and morphine sulfate i.m. in a dose of 20 mg. The dogs were intubated by a cuffed tracheal tube and connected to an Engström respirator and ventilated with a mixture of 50% air and 50% oxygen at a respiration rate of 20 cycles/min. During the short periods of left ventricular cine-angiography the tracheal tube was disconnected from the respirator. After heparinization with 10 000 units i.v., a 8F Millar micromanometer-tipped angiographic catheter was introduced from the right femoral artery into the left ventricle. The micromanometer was calibrated by superposing the micromanometer tracing on the conventional pressure tracing. Prior to insertion, the micromanometer was balanced and zeroed at 37 °C. The frequency response of the recording system including the tiptransducer and DC-amplifier (Electronics for Medicine DR/8) was flat beyond 100 Hz. The resonant frequency of the Millar-tipmanometer was 25–35 Hz. The left ventricular pressure curve was differentiated (dP/dt) by a R–C circuit with a time constant of 0·5 ms. For the assessment of isovolumic contractility and relaxation, max. dP/dt and peak negative dP/dt (min dP/dt) were determined in all eight dogs.

Left ventricular cine-angiocardiography was performed in the right anterior oblique position according to our standard technique[9]. The contrast dye (Urografin® 76%) was injected through the Millar-tipmanometer catheter using a Contrac-injector (Siemens) with an injection rate of 10–15 ml/s. The total amount of contrast dye injected varied between 30 and 45 ml. Monoplane cinefilms (35 mm) were obtained at a speed of 75 frames/s. At the same time the high-fidelity left ventricular pressure at low and high gain, its first derivative, a peripheral lead of the electrocardiogram and a marker signal triggered by the Contrac-injector, indicating the beginning and the end of injection, were recorded on a oscillograph (Electronics for Medicine DR/8) at a paper speed of 200 mm/s. Matching of pressure and angiographic data throughout diastole was performed by determining the largest left ventricular angiographic silhouette, which was considered to represent end-diastolic volume. This maximum volume was matched with end-diastolic pressure and, with end-diastole as a reference, the preceding pressure-angiographic data were matched at intervals of 13·5 ms. It has been shown by Gaasch and coworkers[10] that the maximum diastolic volume coincides within one cineframe with the end-diastolic pressure.

Quantitative analysis of the left ventricular cine-angiograms was carried out according to the 'area-length' method[11]. End-diastolic and end-systolic volumes of the left ventricle were calculated as well as ejection fraction.

Regional shortening was determined in basal, middle and apical segments[12]. These three transverse segments were drawn perpendicular to the longitudinal axis after its quadrisection at equal distances (Fig. 1). The longitudinal axis was inscribed from the aorto-mitral junction to the apex of the left ventricle. Systolic shortening was obtained from the difference of the end-diastolic and end-systolic endocardial circumferential wall length divided by the end-diastolic wall length and multiplied by 100. End-diastolic wall thickness was determined in a right angle to the endocardial surface at the sites where the three segments reached the inferior and the antero-lateral wall (Fig. 1). It was not possible to determine antero-lateral wall thickness at the basal segment, because at that particular site wall thickness was overshadowed by the pulmonary outflow tract. Thus, for the calculation of midwall circumferential wall length and wall stress at the basal segment it was assumed that the thickness of the antero-lateral wall was equal to that of the inferior wall. For the same calculations at the middle and apical segment the antero-lateral and the inferior wall thicknesses were averaged.

Regional myocardial ischaemia was induced by the inflation of a small intracoronary balloon catheter (Fig. 2) developed by Gruentzig[13]. This intracoronary balloon catheter was introduced from the right carotid artery through a short guiding catheter into the left anterior descending coronary artery and placed in the middle or distal part of the descending coronary artery. In six dogs the balloon catheter was proximal and in two dogs distal to the middle segment (Fig. 1). Bulging of the apical myocardial wall was observed in six of the eight dogs and severe hypokinesia in the remaining two dogs. The basal segment remained unaffected by the ischaemia in all dogs and showed enhanced contractions in order to compensate for the decreased shortening of the ischaemic myocardium.

EXPERIMENTAL PROTOCOL

In all eight dogs, left ventriculography was carried out before and during myocardial ischaemia. After the control angiogram a pause of 15 min

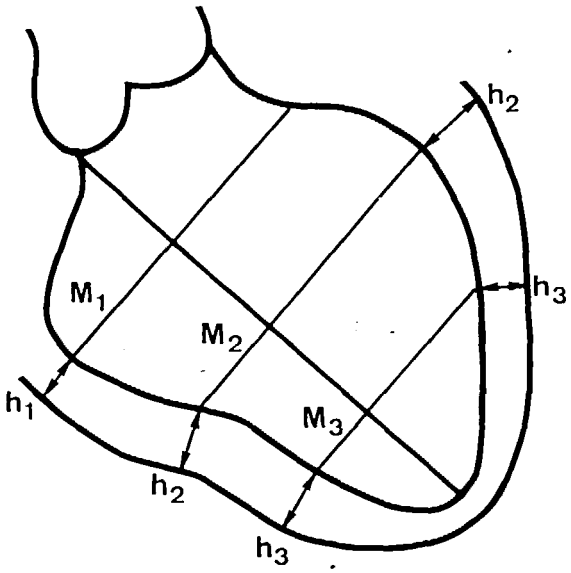

Figure 1 Angiographic left ventricular silhouette at end-diastole. A longitudinal axis is inscribed from the aorto-mitral junction to the apex. Three transverse axes are drawn perpendicular to the longitudinal axis after its quadrisection at equal distances. Wall thickness is determined at a right angle to the endocardial surface at three sites where the three transverse axes reach the inferior and antero-lateral wall. For the calculation of meridional wall stress the inferior and anterolateral wall thickness of the middle and apical segment are averaged, whereas wall thickness at the basal segment is only determined from the inferior wall, because basal wall thickness at the antero-lateral wall is overshadowed by the pulmonary outflow tract. M_1, basal segment; M_2, middle segment; M_3, apical segment; h_1, wall thickness at the basal segment; h_2, wall thickness at the middle segment; h_3, wall thickness at the apical segment.

was usually allowed for dissipation of the haemodynamic and myocardial effects of the contrast dye. Reversible left ventricular myocardial ischaemia was obtained by inflation of the intracoronary balloon catheter for 30 to 90 s. This time interval was determined by the changes in left ventricular end-diastolic pressure and heart rate. Thus, when left ventricular end-diastolic pressure remained constant during ischaemia an inflation time of 90 s was obtained (two dogs), but when the left ventricular end-diastolic pressure increased more than 2 mm Hg or the heart rate rose more than 20% during ischaemia, an inflation time of 30 to 60 s was achieved (six dogs). The second angiogram during myocardial ischaemia was performed at the end of the balloon inflation period. Selective coronary arteriography was carried out in all eight dogs at the end of the study to exclude damage of the transiently occluded coronary artery.

CALCULATIONS

For the evaluation of left ventricular myocardial wall stiffness, determinations of meridional wall stress, midwall circumference, midwall strain and strain rate were made every 13·5 ms starting at the lowest diastolic pressure and ending at the end-diastolic pressure. These parameters were calculated at the same three segments (basal, middle and apical), which were used for the determination of regional systolic shortening. For the calculation of instantaneous wall thickness[14] we assumed that the cross-sectional area of the segmental myocardial wall, determined at end-diastole from the internal left ventricular diameter and the wall thickness, was constant. However, this assumption is not entirely valid, because it assumes no motion in the long axis dimension. To prove this assumption, we determined in six chronically instrumented dogs* left ventricular long and short axes as well as left ventricular wall thickness during control and acute myocardial ischaemia using pairs of ultrasonic crystals. The increase in left ventricular long axis from the lowest diastolic pressure to end-diastole was 5·0 ± 0·2% during control and 4·2 ± 0·2% during ischaemia (given are mean values ± 1 s.e.m.). Left ventricular ischaemic wall thickness was 11·2 ± 1·3 mm at end-diastole during control and 11·1 ± 1·4 mm during ischaemia and decreased by 13·0 ± 1·1% from the lowest diastolic pressure to end-diastole during control and by 8·3 ± 1·2% during ischaemia. Thus, long axis deformation during diastole is in fact small and the resultant error in calculating diastolic wall thickness from the segmental cross-sectional area was, therefore, not great. Direct measurements of the left ventricular wall thickness were not performed in the present study, because the wall thickness changes at 13·5 ms intervals were below the spatial resolution of the angiographic technique. Therefore we calculated instantaneous wall thickness (h) as

$$h = -M/2 + (M^2/4 + A_c/\pi),$$

where M is the internal left ventricular segmental diameter and A_c the end-diastolic segmental cross sectional wall area:

$$A_c = \pi (h_{ed}^2 + h_{ed} M_{ed}),$$

*Unpublished data from the Department of Medicine, Seaweed Canyon, University of California, San Diego, La Jolla (Director: Dr John Ross, jr.).

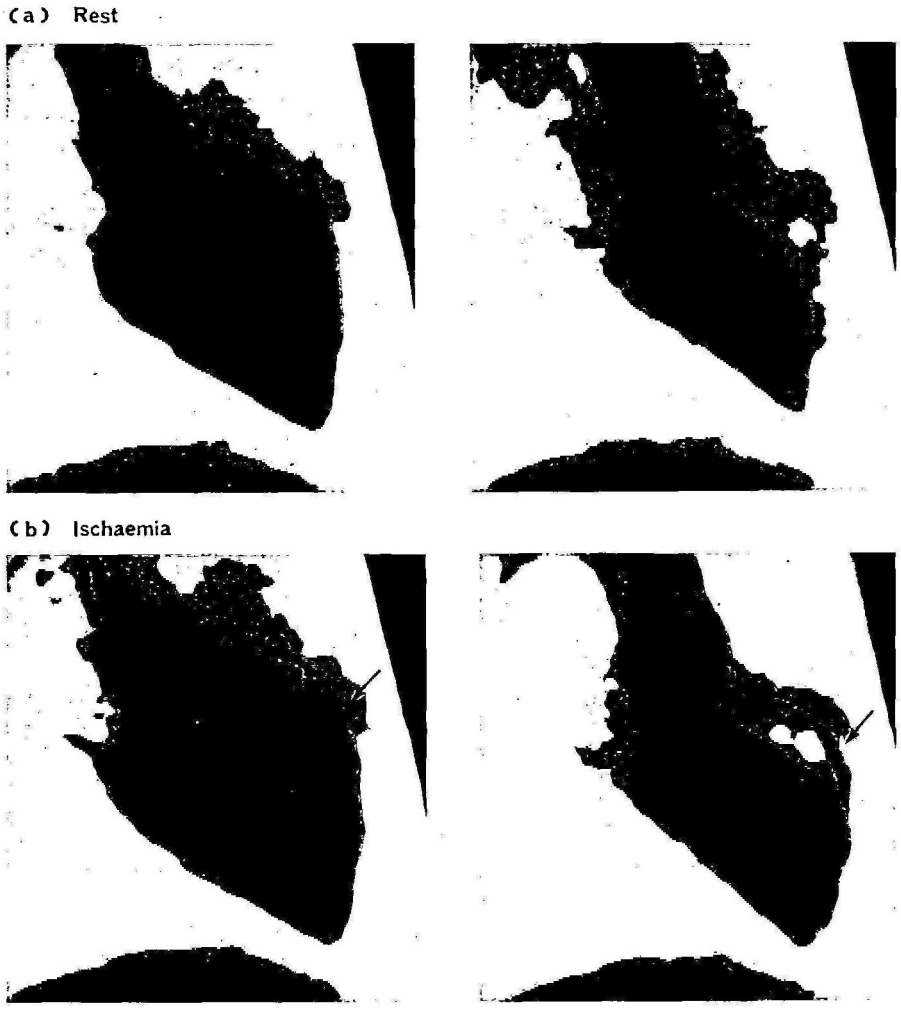

Figure 2 Left ventricular cine-angiograms at rest and during acute myocardial ischaemia. The resting angiogram (a) shows normal contractions without wall motion abnormalities. The angiogram during ischaemia (b) shows, however, hypokinesia of the antero-lateral portion of the left ventricle. The arrow marks the intracoronary balloon in the left anterior descending coronary artery. The angiograms on the left side represent the end-diastolic, the angiograms on the right side the end-systolic left ventricular silhouettes.

where h_{ed} is the end-diastolic segmental wall thickness and M_{ed} the end-diastolic internal left ventricular segmental diameter.

Diastolic segmental meridional wall stress (S) was calculated from the equation:

$$S = PM/[4h/(1 + h/M)],$$

where P is the actual diastolic pressure.

For the calculation of midwall segmental strain (E) the Lagrangian strain definition[15] was used:

$$E = l - l_o/l_o,$$

where l is the actual midwall segmental wall circumference $l = \pi\ (M + h)$ and l_o the diastolic midwall segmental wall circumference at a transmural pressure of 0 mm Hg. However, at ordinary cardiac catheterization it is not possible to obtain true l_o. In order to approximate unloaded muscle length we determined l_o from the stress-midwall segmental circumference relationship (Fig. 3) by extrapolation of the midwall segmental circumference to the very small wall stress (S) of 1000 dynes/

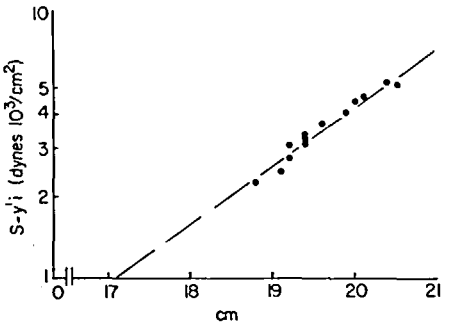

Figure 3 Determination of segmental reference wall circumference l_0 at a transmural wall stress of 1000 dynes/cm², which corresponds to a distending pressure of 0·8 mm Hg. l_0 was determined from the stress-midwall segmental circumference relationship by extrapolation of the midwall segmental circumference to a wall stress of 1000 dynes/cm². The best reference wall circumference to use would have been the diastolic wall circumference at a wall stress of 0 dynes/cm². For practical reasons, however, reference wall circumference at a wall stress of 1000 dynes/cm² was determined, because at lower stresses the long extrapolation distance makes l_0 determination questionable. Moreover, an exponential stress-circumference relationship is unlikely near 0 stress. l_0 was determined by using a viscoelastic model, which was characterized by the equation: $\ln (S-y'\dot{l}) = kl + \ln b$, where S is equal to left ventricular meridional wall stress, $y'\dot{l}$ to the product of diastolic circumferential viscous constant (y') and circumferential lengthening rate ($\dot{l}$) and k, b, equal to viscoelastic constants of circumferential wall stiffness. The three constants (k, b, y') were obtained by using an iteration procedure[14]. $\ln(S-y\dot{l}) = 0{\cdot}51$ 1–8·7; $l_0 = 17{\cdot}1$; $r = 0{\cdot}98$.

cm². This midwall segmental circumference at a stress of 1000 dynes/cm² was called l_0 for the purpose of the present study and served to calculate normalized midwall segmental strain E_n. l_0 was determined by using a viscoelastic stress-circumference model[14, 16] incorporating a parallel elastic and a parallel viscous element. This model was characterized by the following equation:

$$S = be^{ke} + y'\dot{l},$$

where b and k are the viscoelastic constants of circumferential stiffness, y' the viscoelastic constant of circumferential viscosity and l the circumferential lengthening rate ($\dot{l} = dl/dt$). From this equation b, k and y' were determined by fitting the stress-circumference data to a linear regression function $y = ax + b$. The corresponding linear regression equation of the viscoelastic stress-circumference model was therefore:

$$\ln (S - y'\dot{l}) = kl + \ln b.$$

The three constants of this equation (b, k, y') were determined using an iteration procedure [14], where for y' assumed values were inserted into the equation and these values were varied until the best curve fit was obtained. The constants b, k and y' with the best curve fit were considered to be the most accurate data to characterize the diastolic stress-circumference relationship.

The midwall segmental strain rate ($\dot{E}$) was obtained from the equation: $\dot{E} = dE/dt$, where $\dot{E}$ is equal to the first derivative of midwall segmental strain. The normalized midwall segmental strain rate was obtained by $\dot{E}_n = d\dot{E}_n/dt$.

Diastolic myocardial stiffness was determined by the following equation:

$$S = Be^{KE} + y\dot{E},$$

where B and K are the viscoelastic constants of myocardial stiffness and y the viscoelastic constant of myocardial viscosity. The corresponding linear regression equation of the viscoelastic stress-strain model was therefore:

$$\ln (S - y\dot{E}) = KE + \ln B.$$

The three constants of this equation (B, K, y) were determined by the same iteration procedure[14], where y was varied until the best curve fit was obtained. The three constants with the best curve fit were considered to represent best the diastolic functional state of a left ventricular segment stiffness.

Using the normalized strain and strain rate data for the evaluation of myocardial stiffness the constant B of the viscoelastic regression function (= intercept) became constant (= 1000 dynes/cm²) in all evaluated segments and dogs, because the normalized data were based on the diastolic midwall circumference at a common wall stress of 1000 dynes/cm² (l_0). Therefore, the left ventricular diastolic function was characterized by the reference wall circumference l_0, the normalized wall stiffness K_n and the normalized constant of viscosity Y_n.

STATISTICS

The statistical comparison between data of the ischaemic and those of the non-ischaemic state was performed by the paired Student's t-test.

Results

SYSTOLIC FUNCTION PARAMETERS

During acute myocardial ischaemia, heart rate increased significantly from 90 to 108 beats/min (Table 1). Left ventricular end-diastolic and peak systolic pressure did not change significantly, whereas left ventricular systolic ejection fraction decreased from 47 to 31% ($P < 0{\cdot}001$) and left

Table 1 Systolic function parameters during acute myocardial ischaemia.

	Rest	Ischaemia	P
HR (beat/min)	90 ± 5	108 ± 7	<0·02
LVEDP (mm Hg)	7·2 ± 1·2	8·3 ± 1·6	NS
LVSP (mm Hg)	147·0 ± 6·8	142·0 ± 6·3	NS
EF (%)	47 ± 4	31 ± 3	<0·001
EDV (ml)	81 ± 9	91 ± 11	<0·05
SH M_1 (%)	18 ± 3	25 ± 3	<0·02
SH M_2 (%)	27 ± 3	14 ± 2	<0·005
SH M_3 (%)	22 ± 4	2 ± 2	<0·02
max. dp/dt (mm Hg/s)	2273 ± 254	2331 ± 298	NS
min. dP/dt (mm Hg/s)	2576 ± 92	2451 ± 98	NS

HR, heart rate; LVEDP, left ventricular end-diastolic pressure; LVSP, left ventricular peak systolic pressure; EF, left ventricular ejection fraction; SH, endocardial circumferential shortening in a basal (M_1), middle (M_2) and apical segment (M_3); max. dP/dt, maximal rate of rise of left ventricular pressure; min. dP/dt, maximal rate of fall of left ventricular pressure; *P*, probability (paired Student's t-test).
Mean values ± 1 s.e.m. are presented.

ventricular end-diastolic volume increased from 81 to 91 ml ($P < 0·05$). Regional endocardial segmental shortening increased significantly in the basal, but decreased significantly in the middle and the apical segment. Left ventricular max. dP/dt and min. dP/dt showed no significant changes during ischaemia.

DIASTOLIC FUNCTION PARAMETERS

Diastolic reference wall thickness at a wall stress of 1000 dynes/cm² and end-diastolic wall thickness were significantly decreased in the apical segment during ischaemia, but showed no significant change in the basal and the middle segment (Table 2). Diastolic reference wall circumference (l_o) and end-diastolic wall circumference (l_{ed}) increased significantly in the middle segment, but remained unchanged in the basal and the apical segment. Meridional end-diastolic wall stress was significantly higher in the basal and the apical segment during ischaemia, but was normal in the middle segment. The normalized viscoelastic constant of myocardial stiffness K_n was significantly increased in the middle and the apical segment, but normal in the non-ischaemic basal segment. The normalized viscoelastic constant of myocardial viscosity Y_n showed no significant change during acute myocardial ischaemia and remained normal in all three evaluated segments.

Table 2 Diastolic function parameters during acute myocardial ischaemia

		Rest	Ischaemia	P
h_o (cm)	M_1	1·32 ± 0·12	1·23 ± 0·14	NS
	M_2	1·44 ± 0·08	1·35 ± 0·09	NS
	M_3	1·25 ± 0·09	1·07 ± 0·08	<0·005
h_{ed} (cm)	M_1	1·03 ± 0·09	0·96 ± 0·10	NS
	M_2	1·14 ± 0·04	1·12 ± 0·04	NS
	M_3	1·00 ± 0·05	0·89 ± 0·04	<0·01
l_o (cm)	M_1	13·6 ± 0·7	14·3 ± 0·8	NS
	M_2	15·7 ± 0·7	17·3 ± 0·8	<0·005
	M_3	11·0 ± 0·9	11·7 ± 0·9	NS
l_{ed} (cm)	M_1	17·4 ± 0·5	18·7 ± 1·0	NS
	M_2	19·4 ± 0·8	20·1 ± 1·0	<0·05
	M_3	13·7 ± 0·6	13·4 ± 0·6	NS
S_{ed} (dynes 10^3/cm²	M_1	9·7 ± 2·3	13·2 ± 3·1	<0·05
	M_2	9·1 ± 1·8	10·3 ± 2·1	NS
	M_3	6·9 ± 1·7	9·0 ± 2·1	<0·05
K_n	M_1	9·6 ± 1·4	11·8 ± 1·5	NS
	M_2	10·0 ± 0·7	14·2 ± 1·6	<0·02
	M_3	9·8 ± 0·9	12·7 ± 0·8	<0·005
Y_n (dynes 10^3s/cm²)	M_1	0·2 ± 0·1	0·3 ± 0·2	NS
	M_2	0·2 ± 0·1	0·1 ± 0·1	NS
	M_3	0·1 ± 0·1	0·2 ± 0·1	NS

h_o, Diastolic reference wall thickness at a wall stress of 1000 dynes/cm²; h_{ed}, end-diastolic wall thickness; l_o, diastolic circumferential reference midwall length at a wall stress of 1000 dynes/cm²; l_{ed}, end-diastolic circumferential midwall length; S_{ed}, end-diastolic meridional wall stress; K_n, normalized viscoelastic constant of myocardial stiffness; Y_n, normalized viscoelastic constant of myocardial viscosity; M_1, basal segment; M_2, middle segment; M_3, apical segment; *P*, probability (paired Student's t-test).
Mean values ± 1 s.e.m. are presented.

Discussion

SYSTOLIC FUNCTION

In open chest dogs, Théroux and coworkers[17] showed that, during acute left ventricular ischaemia, end-diastolic segment length, determined by ultrasonic crystals, increased and systolic endocardial shortening decreased significantly, whereas in the non-ischaemic control segment both end-diastolic segment length *and* systolic shortening increased. Similar results were found with the angiographic method in the present study, where the end-diastolic wall circumference increased significantly in one of the ischaemic segments and systolic endocardial shortening decreased significantly in both of the ischaemic segments. Moreover, in the non-ischaemic basal segment the slight increase of the end-diastolic wall circumference was associated with a significant increase of systolic

ndocardial shortening. The pressure-derived ıdices of isovolumic contraction (max. dP/dt) and ɔlaxation (min. dP/dt) showed no significant hange during ischaemia in the present study, /hereas Théroux and coworkers[17] have reported a ecrease of both the isovolumic contractility and elaxation. This difference may be explained by wo mechanisms: either the zone of ischaemia was oo small in the present study to affect the pressure-lerived isovolumic indices, or the observed ncrease in heart rate had offset the decrease of both sovolumic indices known to occur with left ventricular ischaemia[17, 18].

DIASTOLIC FUNCTION

It has been shown[17] that during myocardial schaemia, the diastolic pressure-length relationship is shifted to the right of the control curve and that the slope is steeper than during the control state. The latter finding was compatible with an increased stiffness of the ischaemic left ventricular myocardium. This suggestion was, however, offered in a prudent way by Théroux and coworkers[17], because they reasoned that the steepening of the pressure-length relationship could be due to methodological problems, and if chamber geometry and local wall thickness are taken into account for the calculation of the stress-strain relationship, myocardial wall stiffness would eventually not be changed during ischaemia. Our results, based on stress-strain data, show indeed that regional wall stiffness is increased in the ischaemic segments, but remains normal in the non-ischaemic segment. Similar to the results of Théroux and coworkers[17] the diastolic *pressure-circumference* curves of the ischaemic segments (Fig. 4) are shifted to the right and are steepened, whereas the diastolic *stress-strain* curves are shifted to the left and are steepened too. Therefore, it is concluded that regional myocardial wall stiffness is increased during acute myocardial ischaemia.

The change in myocardial wall stiffness during ischaemia may be attributed to several mechanisms extrinsic or intrinsic to the left ventricle. One major point of the study was, however, to rule out some of the *extrinsic* factors — such as altered right ventricular loading conditions and pericardial constriction — by keeping the ischaemic portion small and, therefore, the left ventricular end-diastolic pressure essentially unchanged during myocardial ischaemia. Although left ventricular end-diastolic volume increased significantly during ischaemia, there was no evidence for pericardial constriction, since the left ventricular end-diastolic pressure did not increase more than the increase in end-diastolic volume would have explained. Other mechanisms such as changes in coronary artery perfusion during myocardial ischaemia with an increase in myocardial blood volume and an augmented myocardial turgor ('erectile effect') may result in an increase in myocardial stiffness[7]; however, inflation of an intracoronary balloon is accompanied by a decrease in myocardial blood volume and would, therefore, suggest a decrease rather than an increase in myocardial stiffness. Changes of *intrinsic* properties include incomplete ventricular relaxation, increased viscous resistance and altered passive elastic properties. In the present study, however, incomplete relaxation and increased viscous resistance seem to play a minor role in changes in myocardial stiffness, because both min. dP/dt and the constant of myocardial viscosity were not significantly different at rest and during myocardial ischaemia. Thus, it is concluded that the increase in regional myocardial wall stiffness during ischaemia is due to altered diastolic properties. Crozatier and coworkers[19] demonstrated, by ultrastructural examination of diastolic sarcomere lengths that the end-diastolic sarcomere length of the ischaemic segment is longer than the end-diastolic sarcomere length of the non-ischaemic segment. The stiffness coefficient k of the diastolic pressure-sarcomere length relationship (Table 3) was 6·75 in the non-ischaemic segment and 8·05 in the ischaemic segment. For comparison, the stiffness coefficient K of the diastolic pressure-midwall circumference relationship (Table 3) in our study was 5·94 in the non-ischaemic segment and 8·35 in the ischaemic segment. Thus, the increase in the pressure-circumference stiffness of the middle segment we observed during ischaemia is very similar to that observed by Crozatier and coworkers[19] on the ultrastructural level. They suggested that the increase in sarcomere length during ischaemia is due to a sarcomere overstretch during systole, whereby a loss of basal contractile tone renders the sarcomeres particularly vulnerable to elongation. Therefore, the ischaemic sarcomeres with an increased resting length are operating at a higher level of the pressure-length relationship and require a higher filling pressure for normal diastolic lengthening than the non-ischaemic sarcomeres with a normal resting length.

Thus, it is suggested that the changes in diastolic myocardial wall stiffness during acute ischaemia might be due to the systolic overstretch of the

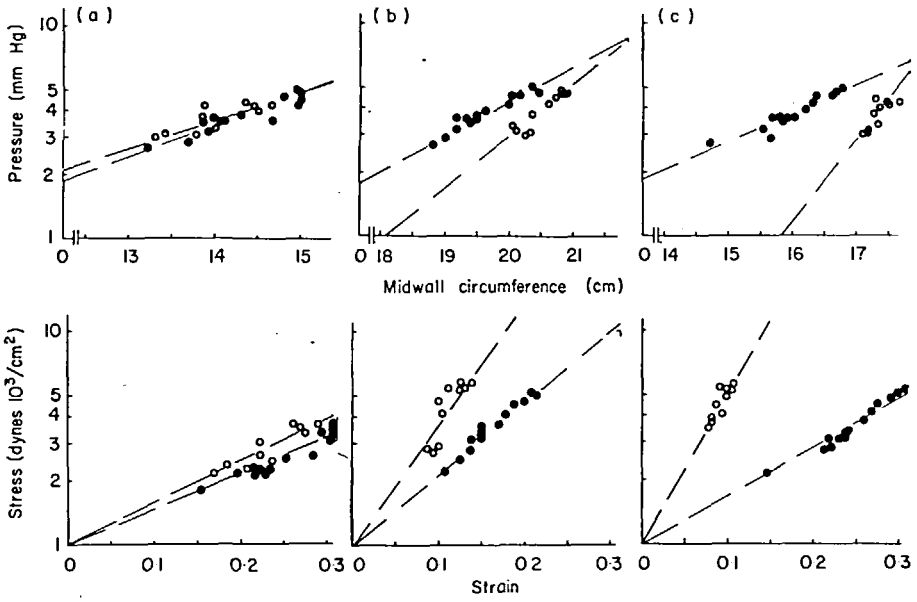

Figure 4. Left ventricular pressure segmental midwall circumference relationship and normalized segmental strees-strain relationship at rest (●) and during myocardial ischaemia (○). (a) Represents the diastolic pressure-circumference and stress-strain relationship in the basal segment, (b) the pressure-circumference and stress-strain relationship at the middle segment and (c) the pressure-circumference and stress-strain relationship at the apical segment. Note that the slope of the pressure-circumference and stress-strain relationship in the basal segment are not changed during ischaemia, but in the middle and apical segment the slope is increased during ischaemia. However, the pressure-circumference relationship shows a shift to the right, whereas the stress-strain relationship shows a shift to the left in the ischaemic segments. This change in the normalized segmental stress-strain relationship during myocardial ischaemia indicates a change in the intrinsic diastolic elastic properties.

Table 3 Pressure-length relationship before and after myocardial ischaemia.

	Sarcomere length				
	LVP	SL	LVP	SL	k
Rest	4·5	2·01	36·5	2·32	6·75
Ischaemia	4·5	2·10	36·5	2·36	8·05

(Crozatier and coworkers[19]).

	Circumferential midwall length				
	LVP	ML	LVP	ML	K
Rest	0·8	1·57	7·2	1·94	5·94
Ischaemia	0·8	1·73	8·3	2·01	8·35

LVP, left ventricular filling pressure (mm Hg); SL, sarcomere length (μ); k, stiffness coefficient of the pressure-sarcomere length relationship; ML, circumferential midwall length at the middle segment ($\mu 10^5$); K, stiffness coefficient of the pressure-midwall length relationship.

ischaemic sarcomeres[19] with an increase in resting length (creep) and a shift of the pressure-sarcomere length relationship to higher filling pressures.

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